REMARKS

The Office Action dated June 28, 2005 has been carefully reviewed, and the following remarks are made in response thereto. In view of the above following remarks, Applicants respectfully request reconsideration and reexamination of this application and timely allowance of the pending claims.

Upon entry of the instant amendment, claims 1-7, 9 and 16 will be under examination. Claim 1 will have been amended, claim 15 will have been cancelled and claim 16 will have been added. Written support for the claim amendments is found throughout the specification and in the original claims. Specifically, support for claim 1 could be found on page 16, line 32 to page 17, line 13. In addition, support for claim 16 could be found on page 20, lines 1 to 13 and in Examples 5 and 13, thus Applicants submit that no new matter has been added.

Claim Rejections under 35 U.S.C. § 102

The Examiner has rejected claims 1, 2, 7 and 9 under 35 U.S.C. § 102(b) as being anticipated by Casterman *et al.* I (WO 94/04678). Specifically, the Examiner asserts that Casterman I discloses the method to produce heavy chain immunoglobulins as claimed in the instant application.

Applicants traverse this rejection. However, in order to expedite prosecution, Applicants have amended claim 1 to recite producing functional heavy chain immunoglobulins in a plastid of a plant. The cited reference does not disclose expression of heavy chain immunoglobulins in a plastid. Thus, in view of the amendment to claim 1, Applicants request that this rejection be withdrawn. Also, since claims 2, 7 and 9 are dependent on claim 1, Applicants also request withdrawal of these rejections.

The Examiner has rejected claims 1, 2, 5, 7 and 9 under 35 U.S.C. § 102(b) as being anticipated by Casterman *et al.* II (U.S. Patent 5,759,808). Specifically, the Examiner asserts that Casterman II discloses the method to produce heavy chain immunoglobulins as claimed in the instant application.

Applicants traverse this rejection. However, in order to expedite prosecution, Applicants have amended claim 1 to recite producing functional heavy chain immunoglobulins in a plastid of a

plant. The cited reference does not disclose expression of heavy chain immunoglobulins in a plastid. Thus, in view of the amendment to claim 1, Applicants request that this rejection be withdrawn. Also, since claims 2, 5, 7 and 9 are dependent on claim 1, Applicants also request withdrawal of these rejections.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 1, 3, 4, 7 and 9 under 35 U.S.C. § 103(a) as being unpatenable over Magnuson *et al.* or Casterman *et al.* I or Casterman *et al.* II in view of Owen *et al.*

Preliminarily, Applicants note that claim 1 was amended to recite producing functional heavy chain immunoglobulins in a plastid of a plant. In addition, Applicants would like to point out that none of the cited references mention or even suggest producing immunoglobulins in the plastid of a plant. In fact, Magnuson *et al.*, Casterman I and Casterman II teach that an endoplasmic reticulum targeting sequence is necessary to produce functional antibodies in plants. Magnuson *et al.* repeatedly indicate that leader sequences (i.e., an ER targeting sequence) are necessary to express functional antibodies in plants:

> i) On page 221, first column, lines 2-3: indicate that antibody accumulation appears to be (partly) dependent "on the presence of functional leader sequences which appear to be necessary for assembly."
>
> ii) On page 221, first column, first full paragraph: cites other studies as underscoring the finding that "a leader sequence was necessary for accumulation of the antibody."
>
> iii) On page 226, second column, last paragraph: describes presence of ER leader sequence as being "crucial."

Both Casterman *et al.* I and Casterman *et al.* II similarly disclose the need to use ER leader sequence to create functional antibodies in plants. Further, Hiatt *et al.* strongly indicates that expression in ER may be required for immunoglobin assembly in plants (see page 77, second column, first full paragraph, esp. first two sentences).

In addition, Owen *et al.* specifically indicates that ER signal sequences "appear to be required" in plants in order to produce functional antibodies – see page 792, first column, under "Discussion." Therefore, Owen *et al.* also teaches away from the claimed invention. Thus, in view of the claim

1 amendment and the fact that none of the cited references teach, or even mention, plastids, Applicants request that this rejection be reconsidered and withdrawn.

The Examiner has rejected claims 1, 3, 5, 7 and 9 under 35 U.S.C. § 103(a) as being unpatenable over Magnuson *et al.* or Casterman *et al.* I or Casterman *et al.* II in view of Le Gall *et al.* Preliminarily, Applicant note that claim 1 was amended to recite producing functional heavy chain immunoglobulins in a plastid of a plant. Concerning Magnuson *et al.*, Casterman I and Casterman II, please refer to the above arguments. As for Le Gall *et al.*, Le Gall specifically indicates (at page 4571, first column, second paragraph under "Discussion") that their vector construction included the leader sequence pelB which would express the scFv via the secretory pathway (i.e., via the ER). Thus, this disclosure further supports that of the above cited references that an ER leader sequence is required. Thus, in view of the claim 1 amendment and the fact that none of the cited references teach the use of plastids, Applicants request that this rejection be reconsidered and withdrawn.

The Examiner has rejected claims 1, 3, 5, 7 and 9 under 35 U.S.C. § 103(a) as being unpatenable over Magnuson *et al.* or Casterman *et al.* I or Casterman *et al.* II in view of Artsaenko *et al.*

Preliminarily, Applicant note that claim 1 was amended to recite producing functional heavy chain immunoglobulins in a plastid of a plant. Concerning Magnuson *et al.*, Casterman I and Casterman II, please refer to the above arguments. As for Artsaenko *et al.*, Artsaenko *et al.* (on page 745, second column) states that they employed an ER targeting sequence as well as a KDEL retention sequence in order to express and retain the immunoglobulin in the ER. The authors further indicate (at page 748, first column, last paragraph) that expression in the ER appears to be necessary to produce active antibody in an amount necessary to produce a measurable effect. Thus, in view of the claim 1 amendment and the fact that none of the cited references teach the use of plastids, Applicants request that this rejection be reconsidered and withdrawn.

Consequently, the all the cited art teaches away from the present invention and a person of ordinary skill would not have been motivated to target expression of heavy chain antibodies as recited in the present application to plastids.

In addition, as discussed on page 6 lines 6 to 14 of the specification as filed, previous attempts to express other types of antibodies in chloroplasts have failed. Further, the specification discloses that expression of scFv in plastids is unstable and has an adverse effect on plastid structure and function (Example 6 and Figure 8). Therefore, there would have been no reasonable expectation of success for a person of ordinary skill to generate the claimed invention. However, expression of functional VHH antibodies was successful (Examples 5 and 13 and Figure 4) with high levels of expression obtained (1.0% and 0.3% of soluble protein extracted – see page 47 lines 17 to 30 and page 56 lines 26 to 34).

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request reconsideration and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, she is invited to telephone the undersigned at her convenience.

Except for issue fees payable under 37 CFR § 1.18, the commissioner is hereby authorized by this paper to charge any additional fees during the pendency of this application including fees due under 37 CFR § 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 CFR § 1.136(a)(3).

Respectfully submitted
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